

HALLUCINOGENS

The Hallucinogens

With a Contribution by T. Weekowitz. By A. Hoffer and H. Osmond. Pp. ix+626. (New York: Academic Press, Inc.; London: Academic Press, Inc. (London), Ltd., 1967.) 200s.

THE hallucinogens, almost totally unknown twenty years ago, currently enjoy a sinister notoriety engendered by their social misuse. This has tended to obscure the most valuable contribution they have made to neurological science. A study of their mode of action has led to advances in biochemistry and pharmacology as well as throwing what little light there is on the biochemical basis of schizophrenia. They have also been used widely in psychotherapy and form an interesting facet of pharmacanthropology. This book surveys all these aspects of the known hallucinogens, covering the literature to 1965. The following fields are covered: origins, chemistry, biochemistry, pharmacology, neurophysiology, psychology, clinical implications and use and anthropology. Naturally some of these are dealt with more fully than others; particularly detailed accounts are given of the psychological and clinical effects of these drugs and interesting details of the use of the plants from which they are derived by various cultures.

Some 150 pages are devoted to adrenochrome and its relatives. The controversies which have raged over this compound are described by the authors, who have long battled in defence of the "adrenochrome theory" of schizophrenia. Some of the bitterness of this dispute is reflected in their comment "adrenochrome, at one time, became a dirty word".

This involves three problems: (1) whether adrenochrome is a hallucinogen; (2) whether it occurs *in vivo*; and, if so, (3) whether it plays any part in the biochemical lesion of schizophrenia. Reports on the psychological effects of adrenochrome have been conflicting, but a recent double-blind study carried out in Czechoslovakia by Grof *et al.*¹ supports the claim that it produces a psychomimetic reaction.

In considering the question as to whether adrenochrome actually occurs *in vivo*, Hoffer quotes twenty authors who found "fluorescent derivatives of adrenaline in body fluids or tissues". However, if one refers to these sources quoted, one finds that there has been some confusion: for example, (i) Utevkii *et al.*⁴ report that whereas brain contains "substances which exhibit the properties of intermediate products of quinoid oxidation of catechol amines" they go on to state "adrenaline, adrenochrome or adrenolutin was not detected". Fischer and Landtsheer⁵ injected the adrenochrome themselves to trace its metabolism, and Bacq *et al.*⁶ and Goldenberg *et al.*⁷ did not detect any adrenochrome at all, but merely used the Von Euler method of estimating adrenaline by converting it themselves to adrenochrome. Fischer and Lecomte⁸ curiously quote Bacq *et al.*⁶ as stating that 10-20 per cent of the injected adrenaline was excreted as an indolic compound—a fact not mentioned in this paper. Green *et al.*⁹ did not actually detect anything but merely suggested a conversion of adrenaline to adrenochrome as a hypothesis to explain the inhibitory action of ferritin on the action of adrenaline on capillaries. Gershenovich *et al.*¹⁰ found adrenochrome only in brains of rabbits dying of oxygen poisoning (exposed to 3.5-6 atmospheres pure oxygen). Three other references were untraceable: I did not consult the rest. Moreover, Hoffer does not quote any of the authors who failed to find adrenochrome in the blood, notably Axelrod². Thus the matter remains quite unresolved. It is still possible that adrenochrome or one of its relatives may be formed in the brain in schizophrenia, although there is no direct evidence to support this. The indirect evidence presented is not very convincing. In our present state of ignorance concerning the biochemistry of schizophrenia it would, however, be

unwise to be dogmatic in any direction. But I would urge in general that workers in this field should recall Popper's dictum that a theory should be tested with the direct aim of trying to refute it. Only by surviving such tests can a theory become valid.

The authors include an attack on the "double-blind" methodology in trials of psychotropic drugs. Although there is much to be said for their criticism of much of the methodology in this field, I remain convinced that the "double-blind" precaution remains quite essential and the failure to observe it has led many investigators wildly astray.

J. R. SMYTHIES

¹ Grof, S., Vojtechovsky, M., Vitek, V., and Prankova, S., *J. Neuropsychiat.*, **5**, 33 (1963).

² Szara, S., Axelrod, J., and Perlin, S., *Amer. J. Psychiat.*, **115**, 162 (1958).

³ Feldstein, A., *Amer. J. Psychiat.*, **116**, 454 (1959).

⁴ Utevkii, A. M., and Osinskaya, V. O., *Chem. Abstr.*, **60**, 14796 (1964).

⁵ Fischer, P., and Landtsheer, L., *Experientia*, **6**, 305 (1950).

⁶ Bacq, Z. M., Fischer, P., and Lecomte, J., *C.R. Soc. Biol.*, **143**, 583 (1949).

⁷ Goldenberg, M., Avonow, H., Smith, A. A., and Faber, M., *Arch. Intern. Med.*, **86**, 823 (1950).

⁸ Fischer, P., and Lecomte, J., *Bull. Soc. Chim. Biol.*, **23**, 569 (1951).

⁹ Green, S., Mazur, A., and Shore, E., *J. Biol. Chem.*, **220**, 237 (1956).

¹⁰ Gershenovich, Z. S., Krichevskaya, A. A., and Alekseenko, L. P., *Chem. Abstr.*, **49**, 10470 (1955).

BIOLOGY OF THE UTERUS

Cellular Biology of the Uterus

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RESEARCH into the anatomy, physiology and biochemistry of uterine and placental function has increased very considerably during recent years. So far, however, few textbooks have attempted even a limited survey of the progress that has been made. Ralph Wynn has brought together fourteen other authors in a very comprehensive review of what he has chosen to call uterine cellular biology. This has enabled him to concentrate attention on the many different aspects of normal uterine function.

Dr S. R. M. Reynolds in a thoughtful opening chapter reviews many of the important advances in the field of reproductive physiology and morphology during the past 40 years. He sets the standard for the excellent chapters that are to follow. He rightly claims "that so large has this field of study become that today a person must of necessity become a student in, rather than of, the subject".

Jack Davies reviews the embryology of the uterus both in the human and other animals. Elizabeth Ramsey describes the vascular anatomy of the uterus, while John Morris discusses the vascular physiology.

The genetic, biochemical and hormonal mechanisms in the regulation of uterine metabolism are considered in reasonable detail by Kenneth McKerns. This chapter includes a consideration of hormone biosynthesis in the ovary and human placenta as well as the steroid relationships between the human foetal adrenal and placenta. These, in fact, are the only aspects of placental metabolism that are discussed, but in a book devoted essentially to the uterus this is acceptable.

The only British contributors to this symposium are Dorothy Needham and Catherine Shoenberg from Cambridge. They provide a very well documented account of the biochemistry of the myometrium listing more than 200 references. Indeed, most chapters include a very up to date and a very complete number of references. Other chapters are devoted to oestrogens, nucleic acids and protein synthesis in uterine metabolism, decidualization, the ultrastructure of the myometrium, the ionic basis of electrical activity in uterine smooth muscle, and hormonal regulation of myometrial activity and its clinical applications.

This book should prove invaluable to all those who are interested in reproductive physiology and biochemistry.